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Hypoxic dilatation of porcine small coronary arteries: role of endothelium and KATP-channels.

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1. The aim of the present study was to determine the cellular mechanims and potential mediators involved in hypoxic dilatation of porcine small coronary arteries. 2. Small coronary arteries were isolated from a branch of the left anterior descending artery of porcine hearts, cannulated with glass micropipettes and studied in a perfusion myograph system. At a transmural pressure of 40 mmHg, the arteries had an internal diameter of 167.8 +/- 6.6 microns (n = 37). 3. In arteries contracted with acetylcholine (ACh), hypoxia (0% O2, 30 min) caused dilatation (86.9 +/- 6.7% relaxation, n = 6) in vessels with endothelium but constriction in endothelium-denuded vessels. 4. Hypoxic vasodilatation occurring in arteries with endothelium was abolished by the KATP channel inhibitor, glibenclamide (0.44 microM), but was not affected by inhibition of nitric oxide synthase (L-NAME, 44 microM) or cyclo-oxygenase (indomethacin, 4.4 microM). 5. Bradykinin evoked endothelium-dependent relaxation that was inhibited by L-NAME (44 microM) but not glibenclamide 0.44 microM). Cromakalim (0.1-0.3 microM), a KATP channel opener, caused relaxation that was inhibited by glibenclamide, but was not affected by L-NAME (44 microM) and/or indomethacin (4.4 microM). 6. Endothelium-removal inhibited vasodilatation evoked by cromakalim, but increased vasodilator responses to the NO donor, SIN-1 (10(-8) to 10(-5) M). 7. These results indicate that hypoxia acted directly on vascular smooth muscle of small coronary arteries to cause contraction. However, this effect was overwhelmed by endothelium-dependent relaxation in response to hypoxia. This relaxation was most likely mediated by release of an endothelium-derived factor, distinct from nitric oxide or prostacyclin, that activated smooth muscle KATP-channels.

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